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(54) Title: MUTATIONS OF VOLTAGE-GATED ION CHANNELS THAT ALLOW THEM TO EXPRESS A VOLTAGE-INDEPENDENT PHENOTYPE AND AN IMPROVED METHOD TO USE THE SAME

Alignment of Voltage-Gated Potassium Channels Relevant Regions

hKv1.1	PYFITLGTFLAEQ-----FGNQKGEQATSLATLRYTRIVRVTRFKLSRHSGK
mKv1.2	PYFITLGTFLAEKP-----EDAQQQQAMSLATLRYTRIVRVTRFKLSRHSGK
Kv1.4	PYFITLGTFLAEQ-----FGNQKGEQATSLATLRYTRIVRVTRFKLSRHSGK
Kv1.3	PYFITLGTFLAEQ-----FGNQKGEQATSLATLRYTRIVRVTRFKLSRHSGK
hKv1.5	PYFITLGTFLAEQ-----FGNQKGEQATSLATLRYTRIVRVTRFKLSRHSGK
ShakerB	PYFITLGTFLAEQ-----FGNQKGEQATSLATLRYTRIVRVTRFKLSRHSGK
rKv3.1	PYFITLGTFLAEQ-----FGNQKGEQATSLATLRYTRIVRVTRFKLSRHSGK
rKv2.1	PYFITLGTFLAEQ-----FGNQKGEQATSLATLRYTRIVRVTRFKLSRHSGK
hKv4.2	PYFITLGTFLAEQ-----FGNQKGEQATSLATLRYTRIVRVTRFKLSRHSGK
hKv1.1	LQILGQTLKASHRELGLLIFFLFGVILFSSAVYFAEAD-----FASHPSSTPDA
mKv1.2	LQILGQTLKASHRELGLLIFFLFGVILFSSAVYFAEAD-----ERSCFPSTPDA
Kv1.4	LQILGQTLKASHRELGLLIFFLFGVILFSSAVYFAEAD-----ECTHPSSTPDA
Kv1.3	LQILGQTLKASHRELGLLIFFLFGVILFSSAVYFAEAD-----DPTSGPSTPDA
hKv1.5	LQILGQTLKASHRELGLLIFFLFGVILFSSAVYFAEAD-----NOOTHPSSTPDA
ShakerB	LQILGQTLKASHRELGLLIFFLFGVILFSSAVYFAEAD-----SEANFPSTPDA
rKv3.1	LQILGQTLKASHRELGLLIFFLFGVILFSSAVYFAEAD-----EDDTPKSTPDA
rKv2.1	LQILGQTLKASHRELGLLIFFLFGVILFSSAVYFAEAD-----SSASKPTSTPDA
hKv4.2	LQILGQTLKASHRELGLLIFFLFGVILFSSAVYFAEAD-----SSASKPTSTPDA
hKv1.1	FWAVVSMITVGYGDMPTTIGGKIVGSCALAGVLTIALPFWIVSNFHYFHRTEDE
mKv1.2	FWAVVSMITVGYGDMPTTIGGKIVGSCALAGVLTIALPFWIVSNFHYFHRTEDE
Kv1.4	FWAVVSMITVGYGDMPTTIGGKIVGSCALAGVLTIALPFWIVSNFHYFHRTEDE
Kv1.3	FWAVVSMITVGYGDMPTTIGGKIVGSCALAGVLTIALPFWIVSNFHYFHRTEDE
hKv1.5	FWAVVSMITVGYGDMPTTIGGKIVGSCALAGVLTIALPFWIVSNFHYFHRTEDE
ShakerB	FWAVVSMITVGYGDMPTTIGGKIVGSCALAGVLTIALPFWIVSNFHYFHRTEDE
rKv3.1	FWAVVSMITVGYGDMPTTIGGKIVGSCALAGVLTIALPFWIVSNFHYFHRTEDE
rKv2.1	FWAVVSMITVGYGDMPTTIGGKIVGSCALAGVLTIALPFWIVSNFHYFHRTEDE
hKv4.2	FWAVVSMITVGYGDMPTTIGGKIVGSCALAGVLTIALPFWIVSNFHYFHRTEDE

(57) Abstract: The subject invention includes mutant voltage-gated ion channels that are open over a wide range of potential differences across membranes. The present invention also includes methods of use of such mutant voltage-gated ion channels in cells with highly negative potential differences across their membranes. One preferred mutant voltage-gated ion channel is a channel with a mutation at the residue homologous to P513 in Kv1.5 and at least one mutation at one of the residues homologous to R400, R403, and R409 in Kv1.5.

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